This report is required by law (7 USX 2143). Failure to report according to the regulations can result in an order to cease and desist and to be sub act to penalties as revived for in Section 21!

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 93-R-0440
CUSTOMER NUMBER: 9199

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

University Of California, San Francisco

(b)(2)High, (b)(7)(F)

(A)
Jan '05
"A" by K Garland
4/10/04
HC

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing or experimentation, or held for these purposes. Attach additional sheets if necessary)

FACILITY LOCATIONS (Sites) - See Attached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (Attach additional sheets if necessary or use APHIS Form 7023A 1

A. Animals Covered By The Animal Welfare Regulations	B. Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals an for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for whom the use of appropriate anesthetic, analgesic, or tranquilize drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reas hsuch drugs were not used must be attached to this repor	F. TOTAL NUMBER OF ANIMALS (COLUMNS C+D+E)
4. Dogs		1	45		46
5. Cats		18	79		97
6. Guinea Pigs		4	36		40
7. Hamsters		62	93		155
8. Rabbits		12	194	5	211
9.Non-human Primates		26	163	8	197
10. Sheep		1	105		106
11. Pigs		2	96		98
12.Other Farm Animals					
13. Other Animals					

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and appropriate Institutional Animal Care and Use Committee (IACUC). A summary of all such exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions, this summary in(brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL (Type or print)

DATE SIGNED

(b)(6), (b)(7)c

11-22-05

APHIS FORM 7023
(AUG 91)

NOV 23 2005

3. The following are the locations where regulated animals were housed or used during the year [Section 2.36(b)(4)]:

(b)(2)High, (b)(7)f

Column E:

The University of California at San Francisco is committed to using laboratory animals in such a way as to minimize pain or discomfort. The Committee reviews each project and many protocols have been redesigned to meet this goal. Attached are the explanations of the procedures producing pain or distress in the animals covered by Subchapter A - Animal Welfare and reported in column E during the period 10/1/04 through 9/30/05 and the reasons anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretations of the research. Separate Optional Column E form (1) is attached. ATTACHMENT to APHIS FORM 7023, Federal Fiscal Year 2004/2005 (93-R-0440).

Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 93-R-0440

2. Number of animals used in this study.

5

3. Species (common name) of animals used in the study:

New Zealand White Rabbit

4. Explain the procedure producing pain and/or distress.

SUMMARY OF EXPERIMENTS DEFINING EXPERIMENTAL CONDITIONS FOR PATHOGENESIS STUDIES OF A VIRULENT *STAPHYLOCOCCUS AUREUS* IN RABBITS

This explanation details methods and approaches used to define experimental parameters for a particularly virulent strain of *S. aureus* used to study staphylococcal disease pathogenesis. In the course of these experiments 5 rabbits infected with this strain died from sepsis and may have suffered unrelieved distress. Our experimental goals were to establish a reproducible and tractable (i.e., not lethal) infection model while minimizing the risk of unrelieved distress and

suffering to the animals. The experimental infection we have relied on is an experimental model of aortic valve endocarditis (AVE), in which a catheter is positioned inside of the heart across the aortic valve and the valve is subsequently infected by injecting the bacterial strain being studied. Three animals in which AVE was induced with this one strain in particular were found dead 14-17h after inoculation. None had clinical signs that would have lead to an earlier endpoint. We therefore sought ways to alter the experimental conditions by modifying the catheterization procedure, as we expected this would attenuate the course of infection and reduce the risk of early and unexpected mortality. The first animal in which the catheter placement step was omitted that was inoculated with this strain initially had bacteria detected in the blood, suggesting a systemic infection. However, this animal cleared the bacteria from the blood, clinically improved, appeared normal over the next several days, and was thought to have cleared the infection. This rabbit unexpectedly died 6 days after infection and autopsy showed that its organs were infected with the experimental strain. This result, however, did confirm that modification of the catheterization procedure had had the desired effect. In further studies to refine our experimental procedures, one other rabbit also lacking the catheter, unexpectedly died. This rabbit manifested no pre-terminal findings that would have allowed an earlier endpoint determination.

Anesthetics were given during the procedure and analgesics were given post operatively. It is debatable whether any of these rabbits actually experienced pain or distress as in humans the studied condition is not reported as painful. Nevertheless, we voluntarily retrospectively report these in Column E.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below).
NA – Retrospective reclassification in Column E.

6. What, if any, Federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102): NA

Column E Explanation

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1. Registration Number: 93-R-0440

2. Number of animals used in this study

2

3. Species (common name) of animals used in the study:

Cynomologous or Rhesus Macaque Monkeys

4. Explain the procedure producing pain and/or distress.

Parkinson's Disease is a common movement disorder caused by the degeneration of dopamine-containing neurons in the basal ganglia, a group of deep brain nuclei. Although the MPTP dosed primate provides one of the best animal models to study this disease and its treatment, the effects of MPTP can vary tremendously between animals. Induction of parkinsonism using MPTP administration invariably leads to some weight loss and a general loss of interest in food. Typically, a severe reduction of appetite or inability to self-feed is transient and can be overcome by hand feeding and provision of appetizing foods. During treatment, these animals may undergo a brief period in which they lose body weight and may require supplemental feeding and parenteral fluid support. One animal is reported in Column E because of weight loss beyond the earlier stated criteria that was secondary to unexpected sequela from a surgical/anesthetic complication. This animal was treated with close attention and has since recovered from weight loss without having to be hand fed. We would not normally report this case as it was not due to the MPTP treatment of the animal. To be conservative in our reporting, however, we will include this animal in Column E.

Another animal we will include in Column E was carried over from the last annual reporting period. In this case, MPTP had a stronger than anticipated effect, leading to severe parkinsonism and prolonged reductions in the ability or motivation to self-feed. The reduced ability to self-feed did not resolve and treatment with Deep Brain Stimulation (DBS) was considered to rescue this animal. The animal's progress was not sufficient to institute DBS therapy and the animal was removed from study. Again, to be conservative in our reporting we retrospectively reclassify the animal in Column E.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below).
NA – Retrospective reclassification due to unanticipated adverse effects.

6. What, if any, Federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102): NA

Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 93-R-0440.

2. Number of animals used in this study.

5

3. Species (common name) of animals used in the study:

Cynomologous or Rhesus Macaque Monkeys

4. Explain the procedure producing pain and/or distress.

The use of the neurotoxin, MPTP, the agent responsible for damage to dopaminergic cells of the substantia nigra, including it's projections to the striatum, produces an experimental model most closely resembling idiopathic Parkinson's disease. In some cases, however, there is also non specific damage to the limbic system which effects the motivation to eat and drink. Here, post MPTP treated animals require supplemental caloric and fluid support. This condition is usually temporary or transient, lasting anywhere from three days to 2-3 weeks, at which point the decision is made to remove the animal from study based on consultation between the attending LARC veterinarian and the primary investigator.
Over the past year, we have experienced a small cohort of animals (5) who experienced weight loss in excess of 15% of pre-MPTP baseline weight. These were geriatric animals (greater than 25 years old) that are particularly sensitive to the associated health challenges of MPTP lesioning. Most of these animals returned to acceptable body weights due to supplemental feeding of high calorie/high protein food items such as ENSURE, hard boiled eggs and peanut butter given as sandwiches or with enrichment devices. One animal remains at a reduced body weight and special permission to keep her on study was requested and granted by the University IACUC committee. She is gaining weight steadily and is in excellent general health otherwise. She is being closely monitored by LARC and the investigator and weighed monthly. One geriatric post MPTP treated animal fell below study body weight criteria and did not respond to supplemental feeding but it was determined that his health problems were not study related and he was euthanized for humane reasons. We voluntarily include this animal in Column E to report conservatively.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below).
NA – Retrospective reclassification in Column E due to unanticipated adverse effects.

6. What, if any, Federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102): NA

Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 93-R-0440.

2. Number of animals used in this study.

1

3. Species (common name) of animals used in the study:

Squirrel Monkey

4. Explain the procedure producing pain and/or distress.

During training on one single day, one animal dropped below the 10% threshold for reporting in Column E by a margin of 17 grams representing a 12.5% weight drop. Veterinarians were consulted and the animal was placed on ad lib water. Her weight increased by the next day to 0.1% below baseline and she has done well since that single day drop and has stayed well above the 10% threshold. We will take a conservative approach and retrospectively reclassify this animal in Column E.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below).
NA- Retrospective reclassification in Column E.

6. What, if any, Federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102): NA

UCSF REPORTABLE IACUC-APPROVED EXCEPTIONS

Species and Numbers:
Monkey, Cynomologous or Rhesus Macaque – 14

Reportable Exceptions – Fluid Regulation – Section 3.83
Fluids are regulated in our animals to motivate them to perform the behavioral task that allows us to investigate questions of how brain circuits generate behavior.

Please note that even these reported animals rarely, if ever, experience a situation where they are not provided potable water twice per day per AWA regulations. We voluntarily report this exception to be conservative in our reporting.

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Species and Numbers:
Monkey, Cynomologous or Rhesus Macaque – 3

Reportable Exceptions – Fluid Regulation – Section 3.83
The goal of our research is to understand the operation of the working brain. One commonly accepted way to do this is to record the behavior of animals and the activity of single neurons during behavior. In our laboratory, and many others around the world, we accomplish this goal by training monkeys to perform simple tasks with fluid or food reinforcements. Eliciting good behavioral performance over a period long enough to acquire meaningful data requires strong motivation on the part of the animal. A successful, humane, and scientifically valid way to attain this level of motivation is through fluid or food reward.

Please note that even these reported animals rarely, if ever, experience a situation where they are not provided potable water twice per day per AWA regulations. We voluntarily report this exception to be conservative in our reporting.

++

Species and Numbers:
Monkey, Owl Monkey - 1

Reportable Exceptions – Fluid Regulation – Section 3.83
Animals are maintained on a daily watering schedule throughout the week. They receive the human equivalent (for a 150 lb human) of 2-3 liters of water per day during the work week. Solid dry food is available ad libitum outside of behavioral sessions all week long, but fruit choices that have high water content are regulated. Water regulation is used so that mild positive appetitive reinforcement can be used for study; most experiments of this class operate under similar regulations, and use mild positive appetitive reinforcement to engage the animals in behavior. In all cases we choose the minimal regulation schedules available to achieve our experimental results. Criteria for exclusion from study follow the UCSF Guidelines and protocol requirements for such studies.

Please note that even these reported animals rarely, if ever, experience a situation where they are not provided potable water twice per day per AWA regulations. We voluntarily report this exception to be conservative in our reporting.

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Species and Numbers:
Monkey, Squirrel Monkey - 2

Reportable Exceptions – Fluid Regulation – Section 3.83
Fluid regulation to elicit specific desired behavior is an absolute requirement for the behavioral training described for this protocol. During training, a monkey will receive liquids only during and following a behavioral session. The animal will be given additional water and/or fruit when returned to its home cage at the end of each training session in an amount adjusted to maintain its weight at an IACUC approved average or level of its normative weight. Modified for the work with squirrel monkeys (New World monkeys), this study will follow the general principles for this type of study and IACUC approved protocol requirements.

Please note that even these reported animals rarely, if ever, experience a situation where they are not provided potable water twice per day per AWA regulations. We voluntarily report this exception to be conservative in our reporting.

Species and Numbers
New Zealand White Rabbits – 5-15
Cynomologous and Rhesus Macaque Monkeys – 22
Squirrel Monkeys – 8

Reportable Exceptions – Innovative Housing – Sections 3.56 and 3.84
In order to provide certain rabbits and nonhuman primates with enhanced physical environments, members of these species are occasionally placed into large "play cages" or "activity modules". Typically rabbits or nonhuman primates are rotated through such cages. The number of such animals varies, but is approximately 20-30 NPH and 5 -25 rabbits over any particular year. The hard surfaces of the play cages or activity modules are spot cleaned and all excreta or disease hazards removed between individuals. These enclosures are sanitized on a normal schedule. Because many of the NHP are paired housed, they constitute a single group of animals for health status. The rabbits are from an SPF vendor. The rotations are often enough that full sanitation between individuals would require frequent dismantling of exercise cages and pens for sanitization and decrease the amount of time it is available for animal use. Individual animals would receive much less opportunity for experiencing this enhanced caging. Clearly the result would decrease this institution's efforts and ability to invoke a creative and positive animal housing experience. Effectively, this is innovative housing approved by the IACUC.

Therefore, this institution reports that as it relates to sanitation between individuals, it varies from Sections 3.56 and 3.84 as they apply to rabbit play cages and NHP activity modules.

University of California
San Francisco
UCSF
A Health Sciences Campus

School of Dentistry
School of Medicine
School of Nursing
School of Pharmacy
The Graduate Division UCSF
Medical Center
The Research Institutes

(b)(6), (b)(7)c

November 21, 2005

ROBERT GIBBENS, DVM
Regional Director – Animal Care
Western Region Office
USDA Animal and Plant Health Inspection Service
2150 Centre Avenue, Bldg B, Mailstop 3W11
Fort Collins, CO 80526-8117

Dear Dr. Gibbens:

I have enclosed APHIS Form 7023, which reports activities of the University of California at San Francisco (Registration Number 93-R-0440, Customer Number 9199) for the federal fiscal year of October 1, 2004 through September 30, 2005.

As there is still no place provided to include the summary of exceptions to the regulations and standards as shown on the Annual Report Checklist when filing on-line, we have chosen to submit the report in it's entirety via hard copy. All information is included in this packet.

Per our prior communication with your Office, we are reporting retrospective reclassifications of certain animals. We are retrospectively reclassifying any non-human primate on a water regulation study that experiences over 10% weight loss in Column E.

We also have established guidelines for non-human primate Parkinson's disease animals that have weight loss greater than 15% relative to a pre-MPTP baseline weight, or a one month period of hand feeding to maintain body weight at greater than 15% of baseline. Any such animals are retrospectively reclassified in Column E.

Clifford Roberts, DVM remains the Director of the Laboratory Animal Resource Center and UCSF Attending Veterinarian.

(b)(7)a, (b)(7)c

NOV 2 3 2005

AEW:kan

Enclosure(s)

cc

(b)(6), (b)(7)c